REMARKS/ARGUMENTS

Claims 67-71, 75, 77 and 95-103 are pending. Other claims have been cancelled previously. Applicants address the Examiner's comments using the same paragraph numbering as the office action.

3. The Examiner alleges that the specification has not been amended to include SEQ ID NOS. However, the Examiner appears to be overlooking the Communication and Preliminary Amendment Under 37 CFR § 1.821-1.825 mailed April 18, 2002, which did amend the specification to include SEQ ID NOS. If the Examiner is missing a copy of this paper or if he has concerns that are not addressed by this paper, he is requested to telephone the undersigned.

6. Claims 67-71, 75 and 77 stand rejected as obvious over Ferrara in view of Cox. The Examiner clarifies that in the previous office action, he was not proposing use of a zinc finger protein as a replacement of Ferrara's discussion of administration of a zinc finger protein isoform but rather as a modification of Ferrara's teaching regarding regulation of VEGF by a transcription regulation factor. The Examiner also alleges that contrary to applicants' assertion, the present specification does not provide evidence that administering a zinc finger protein induces all isoforms of VEGF, but only that it modulates expression of the VEGF-A gene. Applicants maintain traverse.

The Cox patent is not citable as prior art against the present application because of common assignment.

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> 35 USC 103(c).

Here, the Cox patent issued March 18, 2003 and the present application has a filing date of April 30, 2001. Therefore, the Cox patent is citable only under 102(e). The Cox patent and the present application are commonly assigned to Sangamo Biosciences, Inc. The present application was filed after implementation of the above statute (November 29, 1999). Therefore, Cox is not prior art, and the rejection should be withdrawn.

Applicants also note that their previous comments regarding lack of motivation to replace Ferrara's discussion of administration of a VEGF isoform with Cox's discussion of zinc finger proteins are equally applicable to the alternative allegation of obviousness in which Cox's teaching modifies Ferrara's teaching of VEGF regulation by a transcription factor. Ferrara's discussion of VEGF regulation by a transcription factor occurs in the context of a discussion of the mechanism of VEGF regulation. That is, Ferrara is discussing the role of a naturally occurring transcription factor in a natural process. In particular, Ferrara seeks to compare the mechanism of hypoxic regulation of VEGF with that of EPO (see p. 7, first column, second paragraph, first sentence). That VEGF might together with many other genes be regulated by transcription factors in vivo would not have suggested a specific strategy for therapeutic intervention employing zinc finger proteins. The motivation asserted by the Examiner of treating diseases such as ischemia provides reason to perform the therapeutic approach discussed by Ferrara, namely, administering VEGF protein. The asserted motivation would not have impelled the artisan to depart from this approach in favor of a new therapy extrapolated from a discussion of mechanism. Moreover, as was noted in the previous response, Ferrara's observation that the "finding that VEGF protein is able to promote therapeutic angiogenesis even at minute concentrations [citations omitted] suggests that gene therapy may not offer advantages over the recombinant protein" (p. 19, column 1, lines 2-5) would have discouraged, and thereby taught away from efforts to develop alternative therapies by modulation of gene expression. Accordingly, it is maintained that Ferrara did not provide motivation that would have impelled the artisan to the specific combination of modulating angiogenesis using zinc finger proteins represented by the present claims.

With respect to the Examiner's comments regarding isoforms, applicants note that this term is used in the specification (see, e.g., paragraph bridging pp. 18-19) and the art to refer

to splice variants of a given gene. Thus, VEGF-A has a number of splice variants or isoforms, as does VEGF-B. However, VEGF-A and VEGF-B are not isoforms of each other. Therefore, when a zinc finger protein induces expression of an endogenous VEGF gene, all isoforms of the gene are expressed (as discussed in the last response). Indeed the Examiner previously noted that the expression of a plurality of splice variants was inherent in claim 67 (see office action of November 12, 2003 at p. 3, paragraph (5a).

For these reasons, withdrawal of the rejection is respectfully requested.

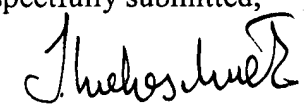
7. Claims 95 and 96-103 stand rejected as obvious over Ferrara and Baird in view of Cox. The Examiner clarifies that he is not relying on Ferrara for contemplating administration of VEGF protein but rather for its discussion of a hypoxia-inducible transcription factor as a means of regulating VEGF. The Examiner also alleges that since administration of a zinc finger protein modulates expression of VEGF, one would be motivated to administer a zinc finger protein with a reasonable expectation of success to treat conditions such as wound healing. Applicants maintain traverse.

The Cox patent is not citable as prior art under 103(c) as discussed above. Moreover, applicants maintain there was a lack of sufficient motivation to combine Ferrara with Cox for the reasons discussed above. Finally, Baird's alleged teaching that VEGF expression is essential for tissue repair would not have provided motivation nor a reasonable expectation of success for the claimed methods. As was noted in the previous response, although upregulation of VEGF may be necessary for wound healing, this does not mean that upregulation is sufficient. Wound healing is a complex process involving many molecules. Unless upregulation of VEGF is a rate limiting step, it is not apparent that delivery of VEGF protein to stimulate aniogenesis, as proposed by Ferrara, would be effective for wound healing. The Baird reference does not attempt to address this issue. In the absence of evidence that delivery of VEGF was sufficient to promote wound healing, it is submitted that one would not have been motivated to combine the teachings of Baird and Ferrara to provide a method of administering VEGF protein to stimulate wound healing, nor would the combination of these references have provided a reasonable expectation of success.

For these reasons, withdrawal of the rejection is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,



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